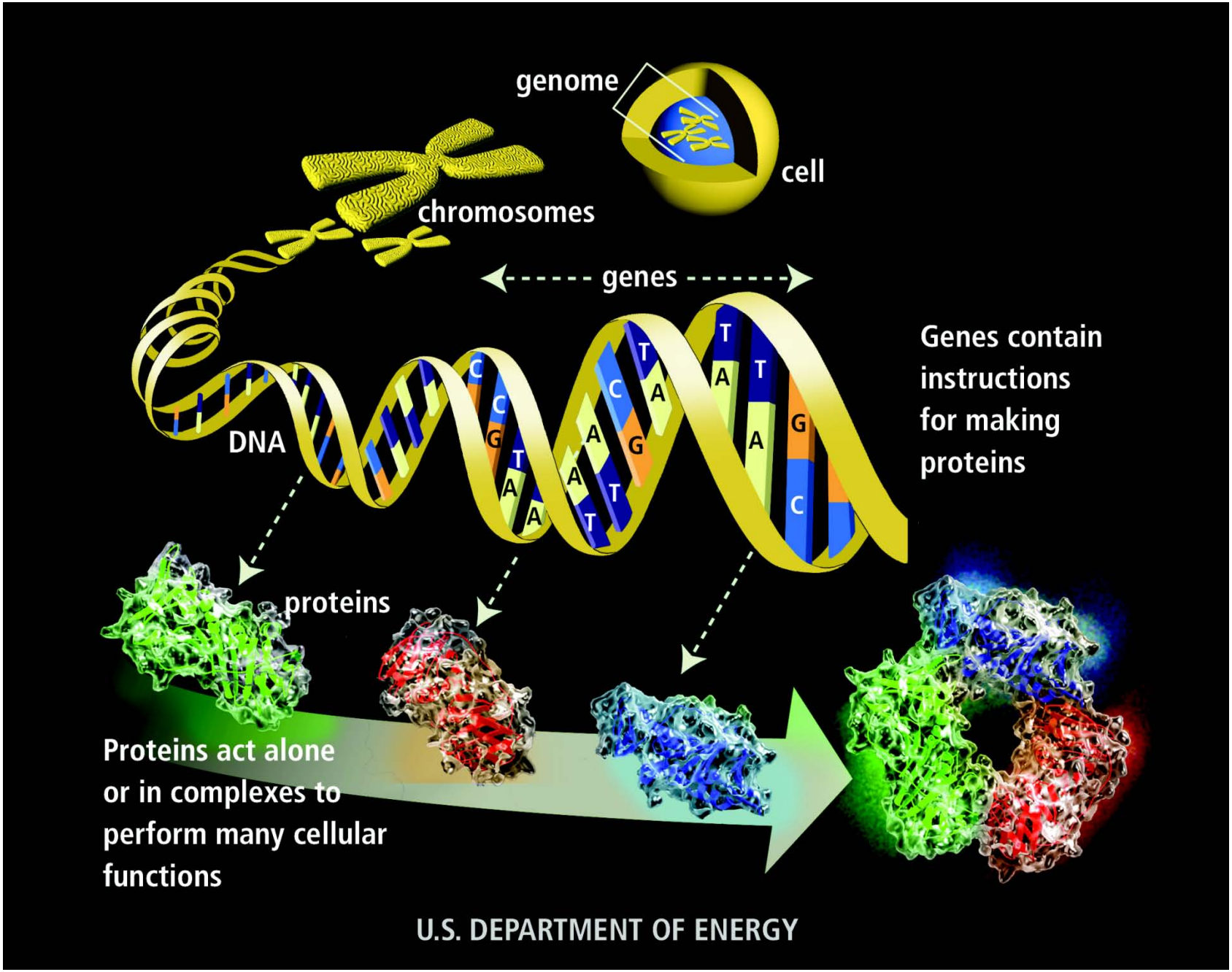
Surviving a Genetic Code

Interprofessional Case Conference

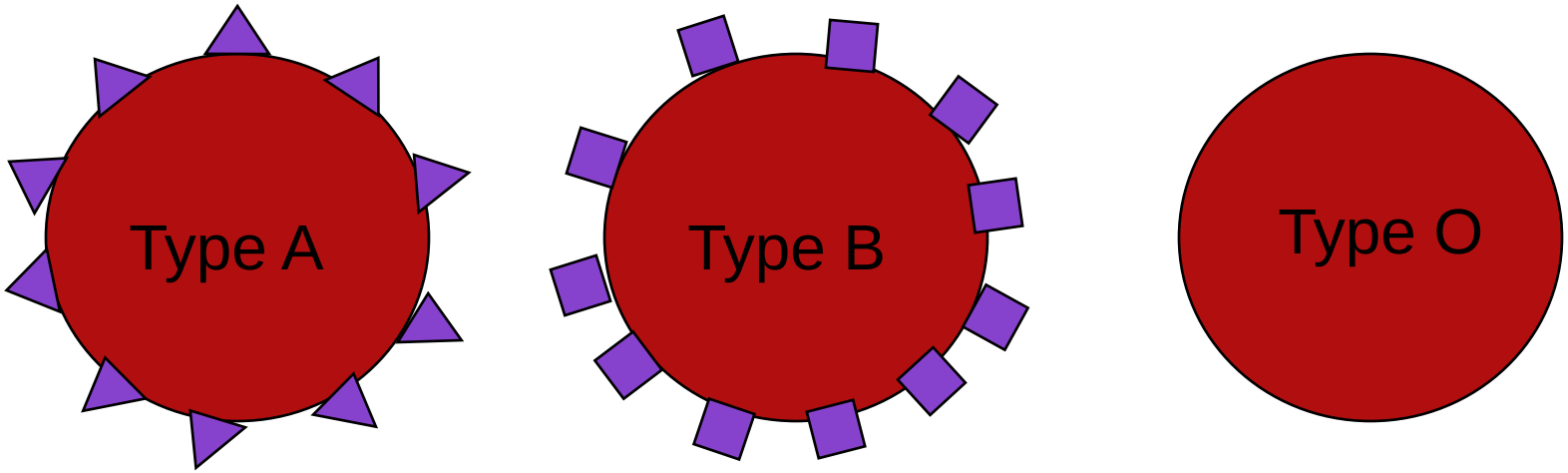
October 23, 2009


genome
cell
chromosomes
genes
DNA
Genes contain instructions for making proteins
proteins
Proteins act alone or in complexes to perform many cellular functions
U.S. DEPARTMENT OF ENERGY

ABO Blood Typing System in Humans

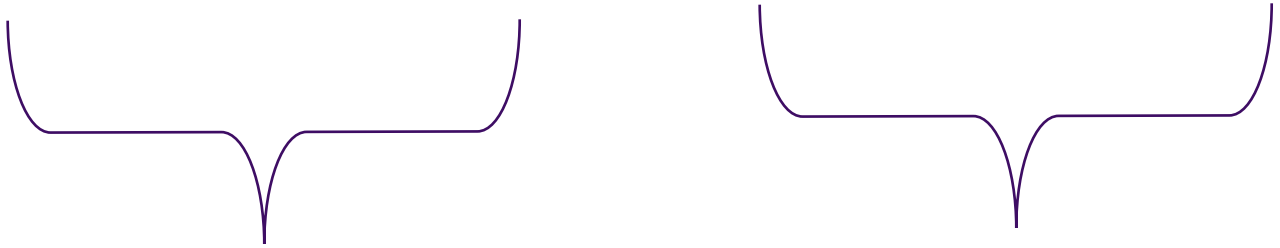
Gene has a “recipe” for an enzyme that adds sugars to a protein found on the surface of red blood cells

3 alleles



AA BB OO

AO BO AB



homozygous

heterozygous

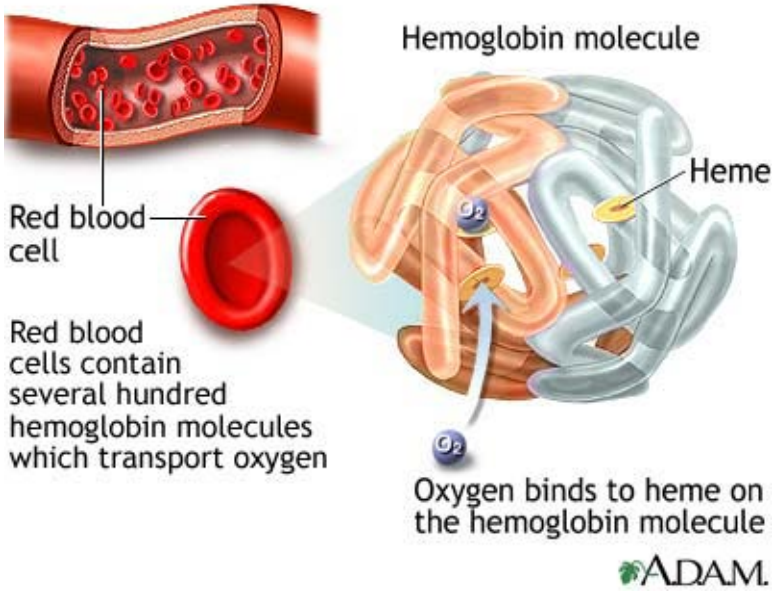
AA → Type A ← AO

BB → Type B ← BO

OO → Type O

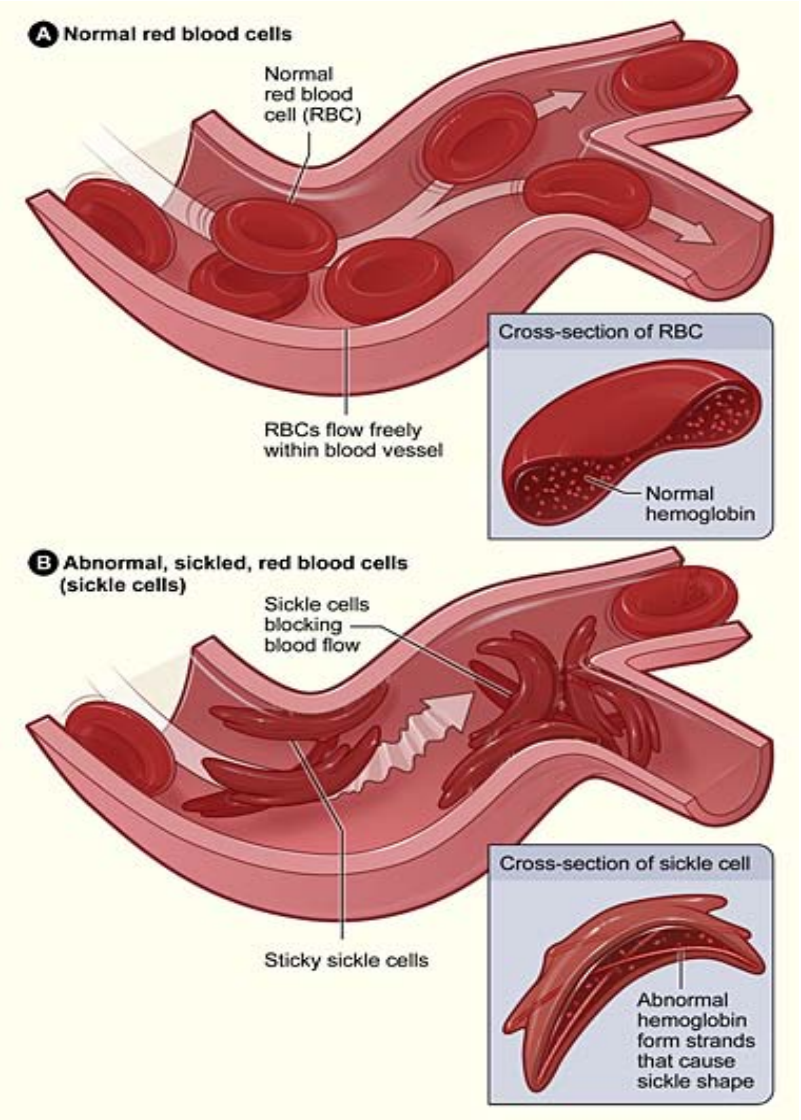
AB → Type AB

Sickle Cell Disease



- Gene contains the recipe to make the protein βglobin, part of the molecule hemoglobin.
- Hemoglobin in red blood cells transports oxygen from the lungs to cells throughout the body

- A mutation, or alteration, in the beta-globin gene results in a defective protein which causes the red blood cells to sickle, stick together, and clog up blood vessels

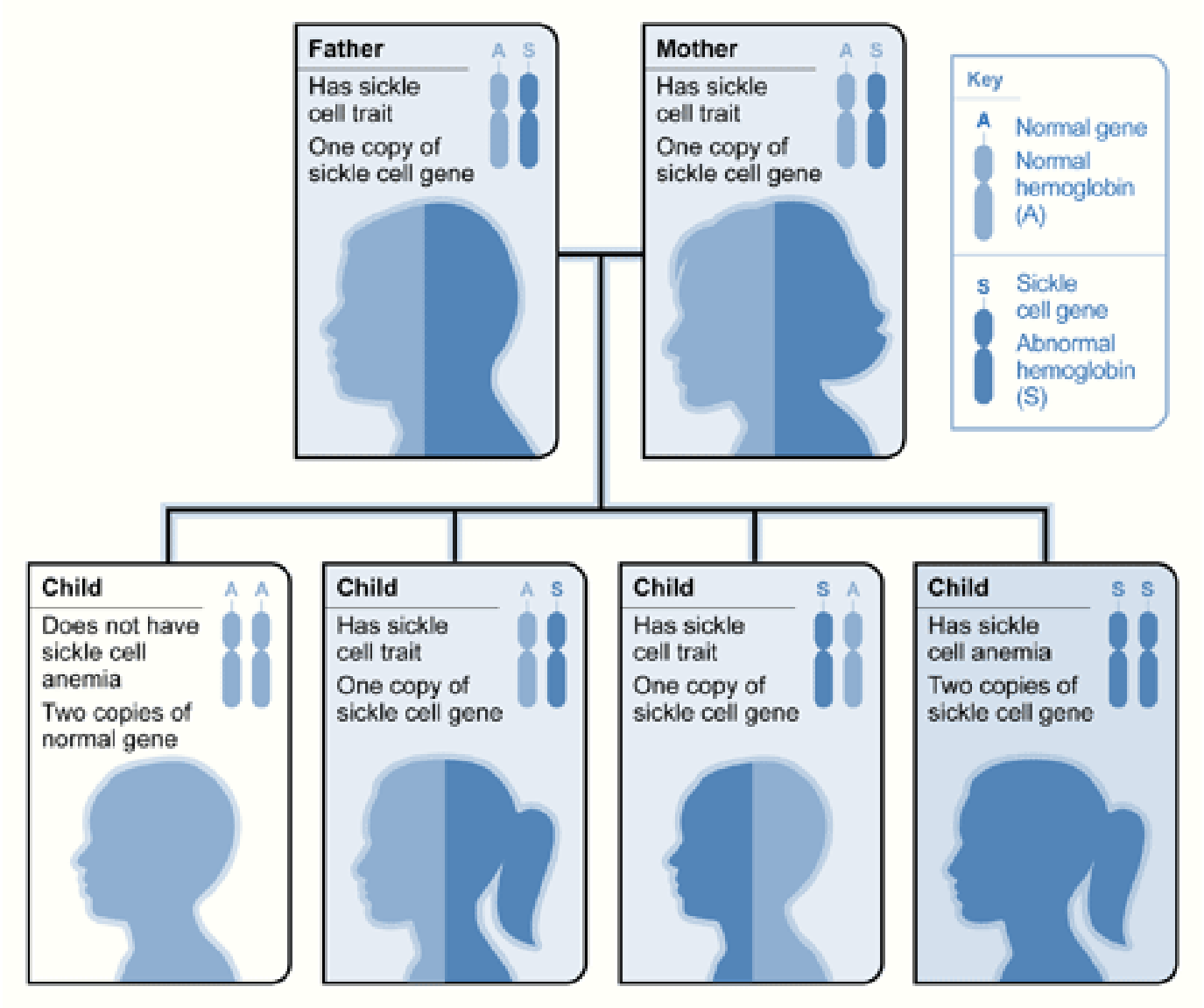


The mutant form of the gene (**a**) is **recessive**, while the normal form of the gene (**A**) is **dominant**, so only individuals who are homozygous for the mutant form of the gene will have sickle cell disease. Individuals who are heterozygous for the gene are said to be *carriers* for sickle cell disease.

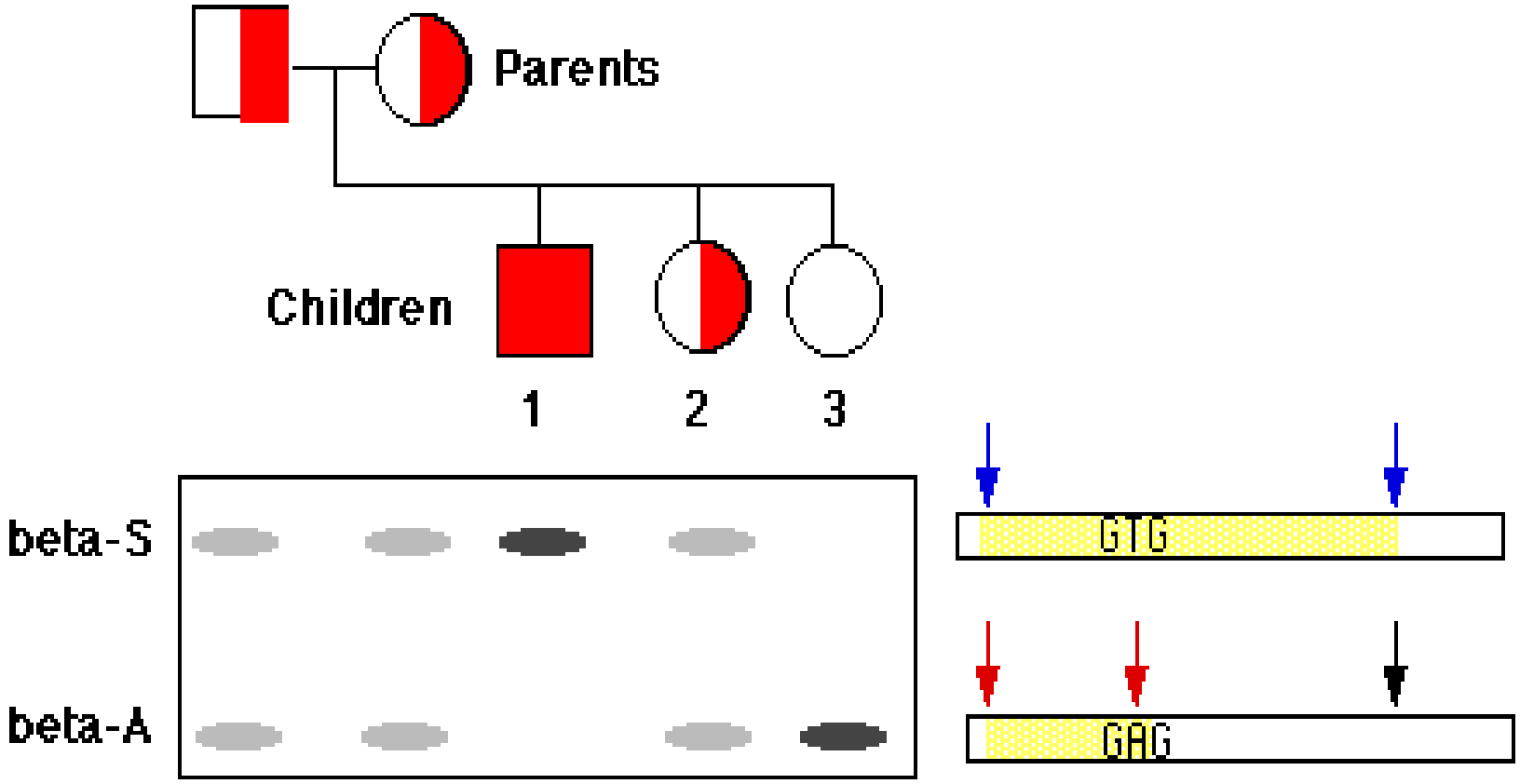
AA → Normal

Aa → Normal (*carrier*)

aa → Sickle cell disease

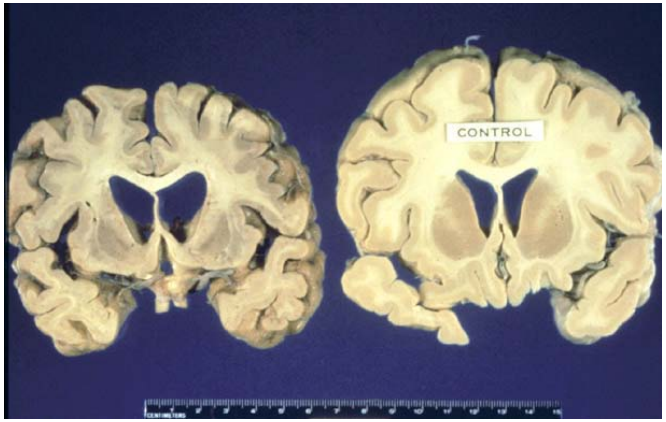

Father
A S
Has sickle cell trait
One copy of sickle cell gene
Mother
A S
Has sickle cell trait
One copy of sickle cell gene
Key
A
Normal gene
Normal hemoglobin (A)
S
Sickle cell gene
Abnormal hemoglobin (S)
Child
A A
Does not have sickle cell anemia
Two copies of normal gene
Child
A S
Has sickle cell trait
One copy of sickle cell gene
Child
S A
Has sickle cell trait
One copy of sickle cell gene
Child
S S
Has sickle cell anemia
Two copies of sickle cell gene

Testing for sickle cell allele



Huntington Disease

- inherited brain disorder that causes uncontrolled movements, mental and emotional problems, and progressive loss of thinking ability (cognition)
- affects about 1 in 10,000 people
- caused by a dominant mutation in the HD gene
- normal gene encodes huntingtin protein



Inheritance of HD

hh x hh → All offspring hh (normal)

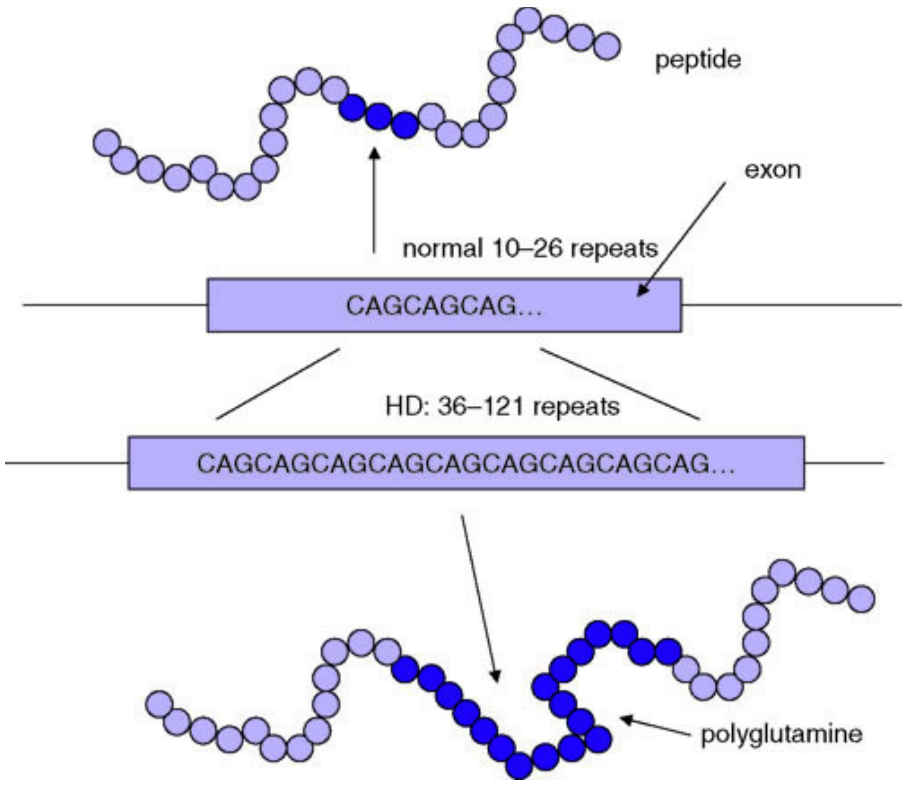
Hh x hh →

50% chance of offspring being hh (normal)

50% chance of offspring being Hh (HD)

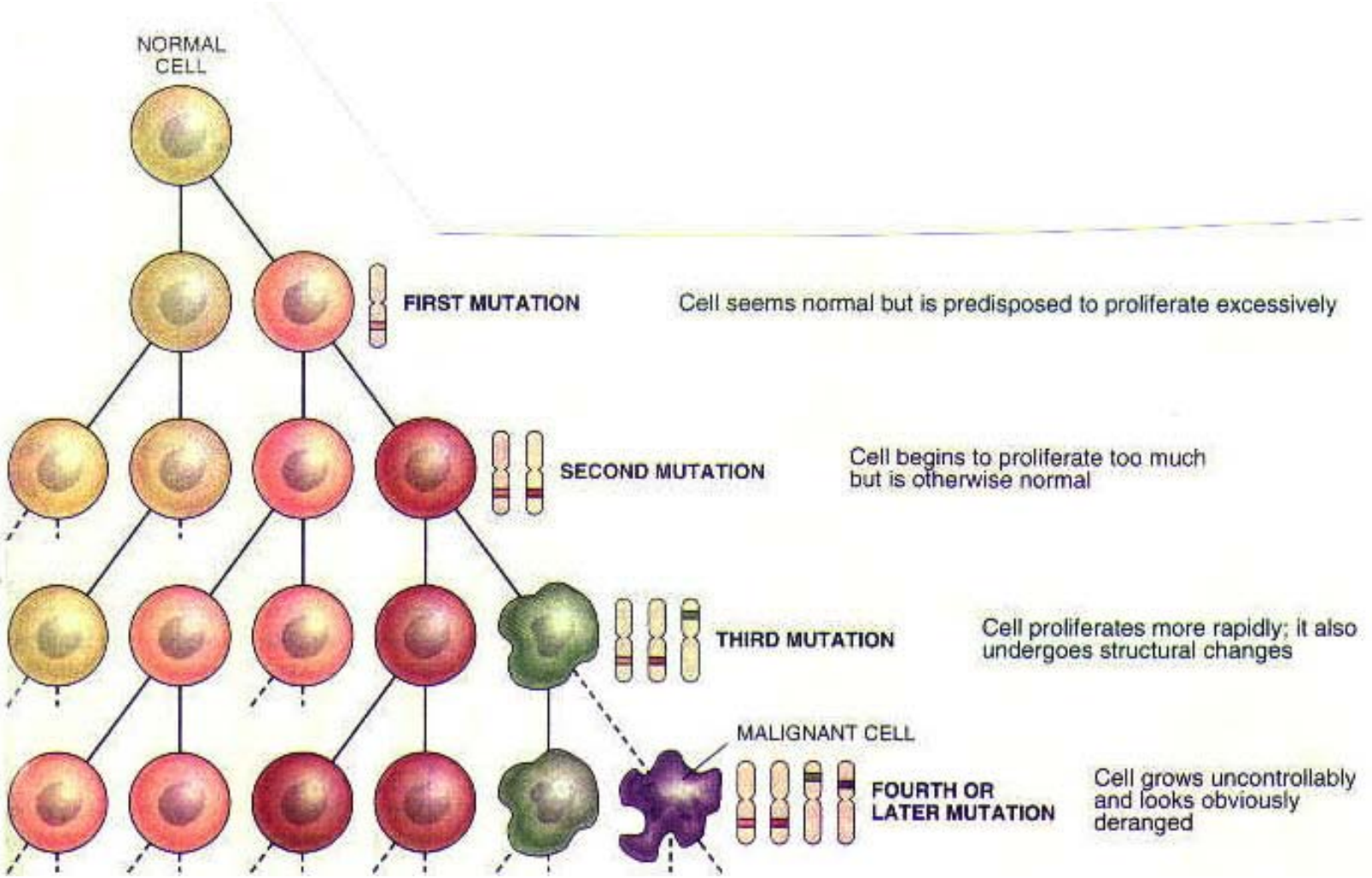
What's happening here?

- The mutation is a short DNA sequence which is abnormally repeated many times, called a CAG repeat expansion
- As the altered HD gene is passed down from one generation to the next, the size of the CAG repeat expansion can increase

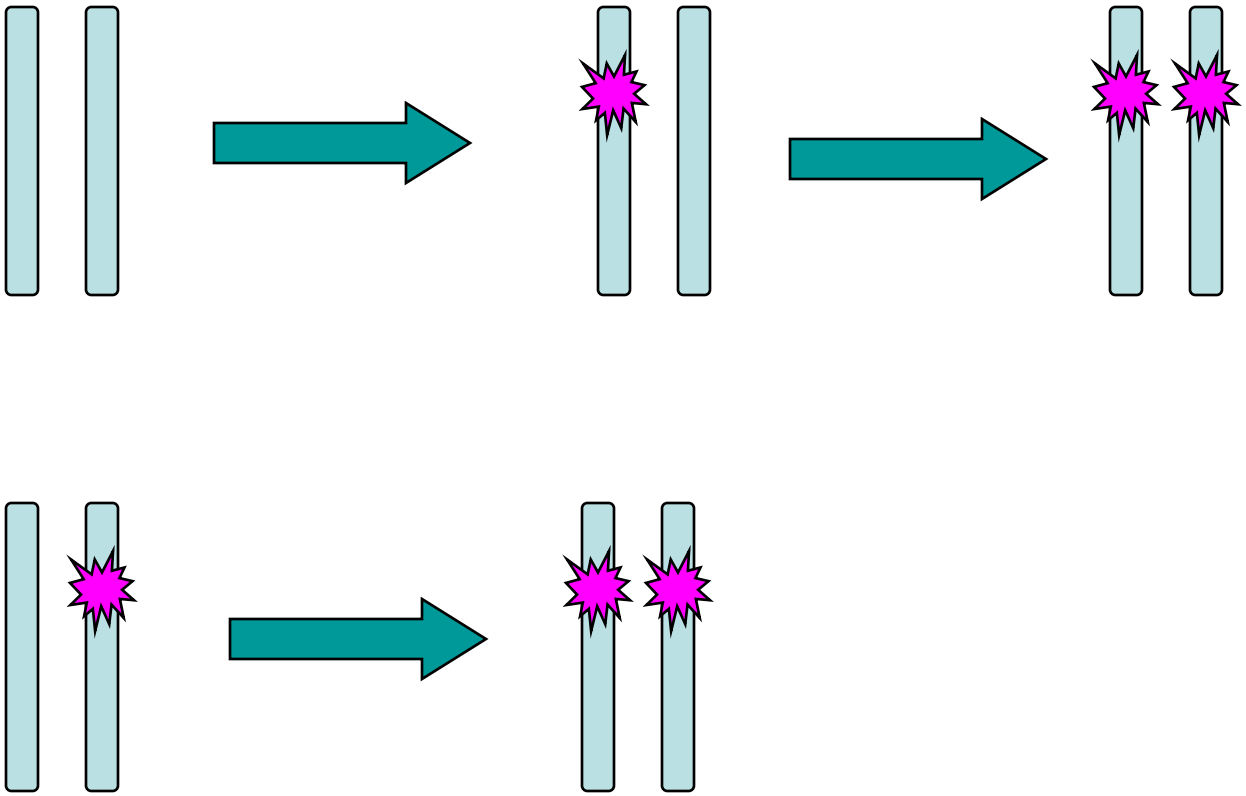


CAG Repeat Size	Median Age at Onset * (years) (95% confidence interval)
39	66 (72-59)
40	59 (61-56)
41	54 (56-52)
42	49 (50-48)
43	44 (45-42)
44	42 (43-40)
45	37 (39-36)
46	36 (37-35)
47	33 (35-31)
48	32 (34-30)
49	28 (32-25)
50	27 (30-24)

Cancer “genes”

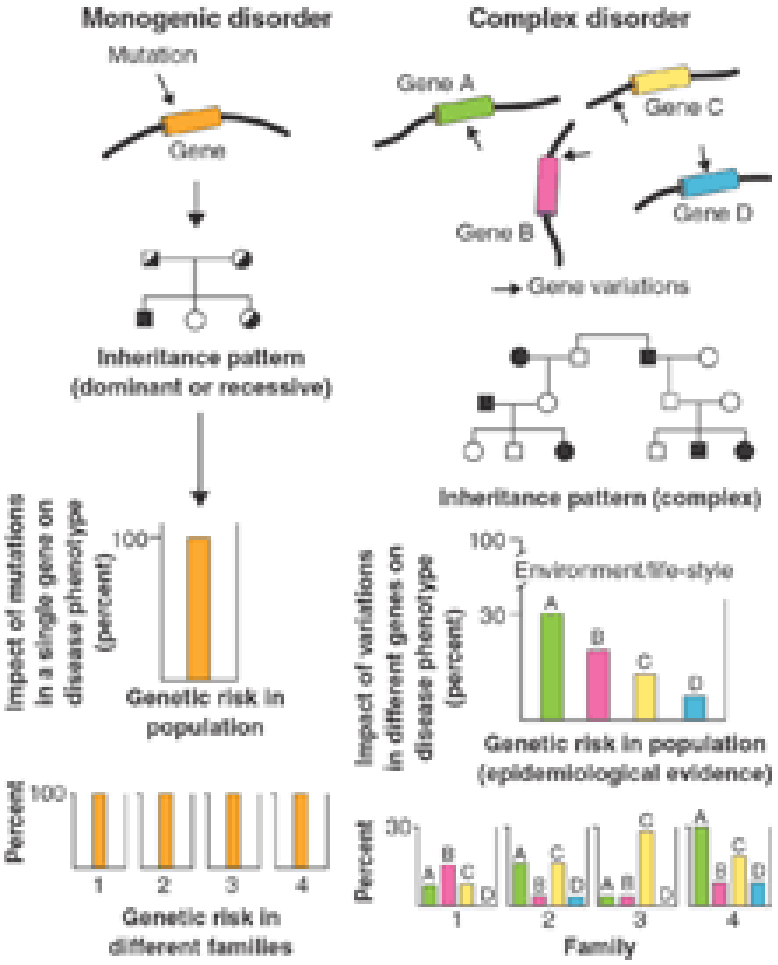


Two-hit hypothesis



Multifactorial inheritance

- characteristics due to interaction of multiple genes AND environmental factors
- conditions run in families, but not in a straightforward fashion
- empiric risks are used to predict the recurrence of a multifactorial disorder
- empiric risk is based on epidemiologic and population studies and on mathematical models



Risk perception

- Your lifetime risk of developing lung cancer is 1 in 9
- You have greater than a 88% of not developing lung cancer
- Your chance of developing lung cancer is twice as high as the general population

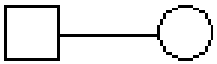
Unaffected male

Affected male

Unaffected female

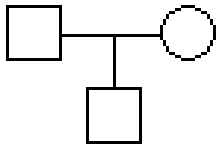
Affected female

Person whose sex is not known

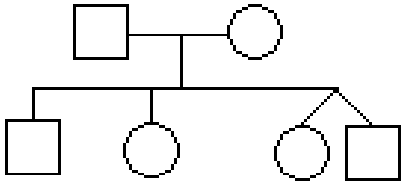


Marriage (mating)

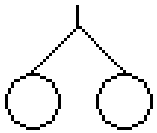
Consanguinous marriage



vertical line = offspring (in this case, son)



A family of four brothers and sisters. The last two are non-identical twins



Identical twins